PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	30.06.2004
Applicant's or agent's file reference: P1317/WOD	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/02716	25.06.2003	28.06.2002

Applicant: THE SECRETARY OF STATE FOR DEFENCE et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P1317/WOD	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/02716	International filing date *(day/month/year)* 25.06.2003	Priority date *(day/month/year)* 28.06.2002
International Patent Classification (IPC) or both national classification and IPC G01N33/543		
Applicant THE SECRETARY OF STATE FOR DEFENCE et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.01.2004	30.06.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Diez Schlereth, D Telephone No. +49 89 2399-7488

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/02716

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-9 as originally filed

Claims, Numbers

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 19

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 19

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/ or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	2,14-17
	No:	Claims	1,3-13
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

   see separate sheet

item V

1.) Reference is made to the following documents:

D1: D. Müller-Schulte & H. Brunner (1995) J. Chromatogr. A 711, 53-60
D2: WO-A-98/54578
D3: JP-A-07 140 143
D4: EP-A-0 480 361
D5: US-A-5,156,971

2.) While the arguments given by the applicant in his letter of 15.06.04 have been considered, the subject-matter of claim 1 and 3-13 (partially, as dependent thereon) is considered to be novel (Art. 33 (2) PCT), but not inventive within the sense of Art. 33 (3) PCT, for the following reasons:

- The wording of claim 1 encompasses embodiments in which the analyte to be detected contains per se a haem moiety (such as a native or glycated haemoglobin molecule);
- Claim 1 defines the pH of the buffer used for releasing haem moieties (the wording of the claim includes examples in which the haem moiety is released with the whole analyte molecule) by the result to be achieved (sufficiently alkaline to release...) instead of by a certain value or range of values (see PCT Guidelines III-4.7). Therefore, in the absence of a clear definition of this (apparently essential) technical feature, it is assumed that the buffer used in D1 (pH = 8.5) is sufficielntly alkaline to release the haem-containing molecules from the magnetic particles while being sufficiently mild for not enabling extraction of inorganic iron from said particles (it is noted that in the present application a buffer of pH 12.5-13.5 is used for releasing haem moieties, see claim 2).

In view of the above comments, the method of claim 1 differs from that of D1 only in that the amount of released haem moieties is measured with a chemoluminescent assay in the presence of luminol (see below).

D1 (closest state of the art as regards this claim) discloses an assay for detection of glycated hemoglobin (gly-Hb) in blood in which magnetic particles comprising Fe_3O_4 are coated with aminophenyl-boronic acid and brought in contact with a sample containing gly-Hb. After binding, gly-Hb is released by washing the particles with an alkaline buffer and the amount of gly-Hb (comprising haem moieties) is measured spectrophotometrically at

414 nm (see experimental part).

However, the selection of a chemoluminescent assay for measuring haem moieties in a sample seems to be an obvious alternative, which falls within the routine practice in this technical field and does not result in any unexpected technical effect. The attention of the applicant is drawn to D2 (example 2), which discloses a magnetic-bead-based assay for detection of gly-Hb similar to that of D1 in which (bound) haem moieties are measured using a chemoluminescent assay in the presence of a lucigenin (a luminol derivative) conjugate; and to D3 (abstract), which discloses a similar assay for detecting occult hemoglobin in feces but using magnetic particles coated with anti-Hb antibody.

The skilled person equipped with the teaching of D1 and D2 (or D3) would consider obvious to detect the haem moieties released in the method of D1 using the chemoluminescence assay of D2 (or D3), thus arriving at a method as claimed in claim 1.

Analogous arguments apply to the subject-matter of claims 3-13 (partially, as dependent thereon), which contain only features which relate to obvious procedural alternatives which fall within the routine practice in this technical field.

3.) Novelty and inventive step (Art. 33 (2) and (3) PCT) could be acknowledged for the subject-matter of claims 2 (complete), 3-13 (partially) and 14-17 (complete), for the following reasons:

Using a buffer with a pH of 12.5-13.5 allows to use a magnetic particle based chemoluminescent assay for accurately measuring the amount of haem-iron present in a sample without having any interferences due to inorganic iron from a magnetic particles.

None of D1-D5 deals with this problem. D1 discloses a magnetic particle based spectrophotometrical assay in which haem-iron is measured without releasing the haem moiety from the analyte molecule. D2 and D3 describe a magnetic particle based chemoluminescent assay for measuring haem-iron without giving any hint about the pH used for releasing haem moieties from the particles. D4 (p. 5, l. 12 to p. 6, l. 30) discloses a chemoluminescent assay in which the luminol reaction is carried out at a pH between 12-13.5 for releasing haem-iron from the analyte molecule. However, this assay does not involve the use of magnetic particles. D5 (abstract) discloses a luminol chemiluminescent assay (without magnetic particles) for the detection of Bacillus anthrax spores.

Analogous arguments apply for the subject-matter of claims 14-17, which relates to a kit that is specially adapted to carry out the method of claim 2.